

use of harm reduction aids. Smokers who cannot quit can be advised to cut down their smoking using NRT, which has a good long-term safety profile.

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POS5-38

EVIDENCE FOR DESENSITIZATION OF $\beta 2$ CONTAINING NICOTINIC ACETYLCHOLINE RECEPTORS IN REGULATING BODY WEIGHT IN OBESE MICE

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Nicotine's effects on food intake (FI) and body weight (BW) are well documented; however, the relevant nicotinic acetylcholine receptors (nAChRs) mediating these effects are not firmly established. Using both pharmacological tools and knockout mice, we demonstrate an important role for desensitization of $\beta 2^*$ nAChRs in the control of energy homeostasis. (Note: The asterisk indicates that the α subunit associated with this $\beta 2$ subunit has not yet been identified, but is most likely an $\alpha 4$ and/or $\alpha 6$ subunit.) In this study, we set out to: (1) identify the nAChR subtype involved in FI and BW; (2) determine whether FI and BW reduction produced by nicotinic drugs are due to activation or desensitization of nAChRs. To identify the nAChR subtype, we tested the effect of sazetidine-A (SAZ-A), a relatively selective ligand for $\beta 2^*$ nAChRs, on FI and BW in 15 week-old obese mice. SAZ-A administered twice daily (3 mg/kg; SC) decreased FI and BW. To assess whether these effects were consistent with desensitization, SAZ-A was administered to non-obese mice by osmotic minipump. This method of sustained delivery of SAZ-A, which causes continuous desensitization of $\beta 2^*$ nAChRs, reduced FI and decreased the gain in BW. Moreover, a similar effect was obtained by administering dihydro- β -erythroidine (DH β E), an antagonist of $\beta 2^*$ nAChRs. In contrast to these results in wild-type mice, SAZ-A did not affect FI or BW in $\beta 2$ knockout mice ($\beta 2^{-/-}$). Importantly, we observed that adult $\beta 2^{-/-}$ mice (both male and female) gained less weight over time and had a leaner phenotype than wild-type controls, a finding that has not been reported previously (possibly because most previous studies used younger mice). Together, these results indicate a $\beta 2^*$ nAChR subtype is essential to the effect of SAZ-A on FI and BW. Moreover, these results suggest that $\beta 2^*$ nAChRs contribute to regulation of BW in mice. These findings may be of interest to researchers studying targets to treat obesity and/or investigating brain circuitry regulating FI. Lastly, our data suggest that desensitization of $\beta 2^*$ nAChRs by drugs such as SAZ-A may serve as an effective therapeutic approach for controlling weight gain.

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HIGHLIGHTED FINDINGS FROM WAVE 1 OF THE POPULATION ASSESSMENT OF TOBACCO AND HEALTH (PATH) STUDY

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The National Institutes of Health, through the National Institute on Drug Abuse, is partnering with the Food and Drug Administration's Center for Tobacco Products to conduct the Population Assessment of Tobacco and Health (PATH) Study, under a contract with Westat. The PATH Study is an address-based nationally representative, longitudinal cohort study of 45,675 adults and youth in the United States aged 12 years and older. The study uses Audio-Computer Assisted Self-Interviews for adults and youth to collect information on tobacco-use patterns across tobacco products on the U.S. market; risk perceptions and attitudes towards tobacco products including emerging tobacco products; and tobacco initiation, cessation, and relapse behaviors. Additionally, the PATH Study collects biospecimens among consenting adults aged 18 years of age and older for future evaluation of biomarkers of exposure and harm related to tobacco use. Expanding upon the interim Wave 1 data presented at SRNT in 2015, we will provide a short overview of

the design and methods of the PATH Study and then provide highlighted results from the entire Wave 1 sample. We will report on domains related to the appeal, addictiveness and harm of tobacco products, including youth susceptibility, experimentation and use of products; harm perceptions and exposure to marketing as well as adult use and harm perceptions of tobacco products. Additional behavioral data on selected tobacco products will be discussed. The presentation will conclude with a summary of Wave 2 and Wave 3 data collection progress and the next steps for the PATH Study, information on how researchers can access Wave 1 PATH Study questionnaire data through a Restricted Use File, and questions from the audience.

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NICOTINE WITHDRAWAL INDUCES NEGATIVE CORRELATION IN RESTING CONNECTIVITY BETWEEN INSULA AND EXECUTIVE CONTROL NETWORKS IN SMOKERS

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Because the insula is central in detecting and acting upon internal states and external stimuli, understanding how it interacts with other brain regions to modify behavior may help elucidate neural mechanisms of nicotine withdrawal. The insula is a key node of the salience network (SN), the large-scale brain network implicated in switching attention between executive control (ECN) and default mode (DMN) networks. The ECN, which is activated in effortful cognitive processing, is anticorrelated with the DMN, which deactivates during externally-oriented tasks. Nicotine withdrawal alters interactions among these networks such that DMN-insula connectivity is upregulated in abstinent smokers. Yet, the downregulation predicted between insula and ECN in withdrawn smokers has not been demonstrated. Resting-state BOLD data were acquired from 18 smokers at baseline smoking and again following approximately 48 hours of smoking abstinence. Based on previous literature, we derived 3 regions of interest in the insula (dorsal anterior, ventral anterior, and posterior) and conducted seed-based analyses examining the functional connection between each insula seed and each of the 3 networks of interest-SN, ECN, and DMN. The contrast of abstinence minus baseline showed upregulated connectivity between dorsal insula and DMN and downregulated connectivity between ventral insula and ECN during abstinence. Surprisingly, the magnitude of both correlations increased in abstinence. The connectivity between insula and DMN became more positive, while the correlation between insula and ECN became negative. Instead of seeing the predicted switch of strong positive insula-ECN connectivity at baseline for strong positive insula-DMN connectivity in abstinence, results suggest increased, yet directionally opposite, connectivity between insula and both ECN and DMN in abstinence. This pattern suggests in smokers the absence of nicotine enhances connectivity in multiple brain networks. Thus, future treatments may aim to downregulate these connections simultaneously.

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E-CIGARETTE USE IN VA SERVICE USERS WITH PSYCHIATRIC AND SUBSTANCE USE DISORDERS

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Individuals with mental illness and substance use disorders smoke at elevated rates and tend to have greater difficulty quitting smoking as compared to the general population. Some believe that e-cigarettes reduce harm associated with smoking, but little is known about e-cigarette use, perceptions, and motivations